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MESOSCOPIC NON-EQUILIBRIUM THERMODYNAMICS

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ABSTRACT. Basic concepts like energy, heat, and temperature have acquired a precise meaning after the development of thermodynamics. Thermodynamics provides the basis for understanding how heat and work are related and with the general rules that the macroscopic properties of systems at equilibrium follow. Outside equilibrium and away from macroscopic regimes most of those rules cannot be applied directly. In this paper we present recent developments that extend the applicability of thermodynamic concepts deep into mesoscopic and irreversible regimes. We show how the probabilistic interpretation of thermodynamics together with probability conservation laws can be used to obtain kinetic equations describing the evolution of the relevant degrees of freedom. This approach provides a systematic method to obtain the stochastic dynamics of a system directly from the knowledge of its equilibrium properties. A wide variety of situations can be studied in this way, including many that were thought to be out of reach of thermodynamic theories, such as non-linear transport in the presence of potential barriers, activated processes, slow relaxation phenomena, and basic processes in biomolecules, like translocation and stretching.

1. Introduction

Irreversible processes taking place in large-scale systems are well described by non-equilibrium thermodynamics [1]. The theory applies to a coarsened description of the systems which ignores their molecular nature and assumes that they behave as a continuum medium. Under these circumstances, the description does not depend on the size of the system. Scaling up the size does not lead to new behaviors. Irreversible processes taking place in a small vessel or in an industrial plant can then be analyzed using the same conceptual framework. When scaling down the size of the system, its molecular nature manifests itself. The coarsening is no longer valid due to the presence of fluctuations in the quantities used in the description. One then reaches a very different scenario in which non-equilibrium thermodynamics may only describe the evolution of the mean values of those quantities but does not completely characterize their actual values. In small systems, such as clusters or biomolecules, otherwise small fluctuations in large-scale systems can be large to the extent that they may become the dominant factor in their evolution. Small is different. The so-called meso-structures, entities whose sizes are in between those of particles and objects sizes, are examples of small systems undergoing assembling, impingement and pattern formation processes in which fluctuations may play a very important role. The knowledge of the functionality of molecular motors, small engines present in many biological systems, and the possibilities of manipulation of matter at small scales to improve

performance which constitutes the basic objective of new disciplines as nanoscience and nanotechnology, requires a thermodynamic characterization of the system [2].

Our purpose in this paper is to show that the evolution of small systems can be analyzed by using the method established by non-equilibrium thermodynamics to study irreversible processes taking place at large scales. The new theory proposed to this end, called mesoscopic nonequilibrium thermodynamics (MNET) [3], [4] can be used to analyze the irreversible behaviour of the meso-structures and to explain processes such as nucleation, growth and active transport in biological membranes which cannot be explained by conventional non-equilibrium thermodynamics due to their inherent nonlinear nature and to the important role played by fluctuations.

The paper is organized as follows. Section 2 presents the main ideas of equilibrium thermodynamics of small systems. In Section 3 we proceed with the study of small systems outside equilibrium by introducing the mesoscopic non-equilibrium thermodynamics theory. In Section 4 we show that the theory provides non-linear constitutive equations, such as the law of mass action. In Section 4 we present some applications of the theory. Finally, in the conclusion section we summarize our main results and discuss about perspectives of the theory presented.

2. Thermodynamics of small-scale systems

Thermodynamics [5] can only be applied to systems with an infinite number of particles distributed in an infinite volume with a constant density, a situation referred to as the thermodynamic limit. Under these circumstances one may adopt a coarse description of the system ensuring the existence of extensive quantities and justifying the absence of fluctuations. The thermodynamic limit [6] can be asymptotically approximated through statistical mechanics and the results from different statistical ensembles converge. It is then said that thermodynamics deals with large-scale systems.

The lack of a thermodynamic limit has important consequences for the behavior of the system. Scaling down the size leads to a very different scenario, in which contributions to the energy of the system not present in the thermodynamic limit, such as surface energy, may show up, thereby breaking extensivity and making a normal thermodynamic treatment impossible. A typical example is a small cluster of N particles whose Gibbs energy is given by [2]

$$G = \mu N + aN^{\beta} \tag{1}$$

with μ the chemical potential, a an arbitrary function of the intensive parameters and $\beta < 1$ an exponent. When the cluster contains a large number of particles, the second contribution becomes much smaller than the first and can be neglected. At this limit one obtains the well-known thermodynamic relation $G \cong \mu N$ for which the chemical potential is the Gibbs energy per particle. On the other hand, for clusters containing a smaller number of particles both contributions must be considered, which makes the Gibbs energy non-extensive. As a consequence thermodynamics does no longer apply. Without a coarse description, fluctuations become important and play a role in the characterization of the system.

Despite this relevant feature, a thermodynamic treatment of small system is still possible. The way to proceed was proposed by Hill [2] for systems at equilibrium and was

subsequently applied to different situations such as biochemical cycle kinetics [7], [8], open metastable systems [9], entropy-enthalpy compensation effects [10], and critical behavior of ferromagents [11]. It was later referred to as nano-thermodynamics [12]. Given a small system, the ensemble of many of its replicas becomes a large system having the usual thermodynamic behavior. To restore the form of the Euler equation, the expression of the Gibbs energy in terms of the chemical potential, one can express the Gibbs energy as

$$G = \widehat{\mu} N \tag{2}$$

where the chemical potential $\widehat{\mu}$, according to Eq. (1), is given by

$$\widehat{\mu} = \mu + aN^{\beta-1} \tag{3}$$

Both chemical potentials thus coincide at the thermodynamic limit. It can also be shown that thermodynamic quantities defined for different ensembles, may not be equivalent.

Thermodynamics of small systems has been formulated at an equilibrium state. In many experimental situations, however, instead of being in a quiescent state, the system evolves in time adopting different non-equilibrium configurations. This situation is commonly found in kinetic processes such as nucleation [13] and growth [14] of small clusters, in noncovalent association between proteins [15] and in active transport through biological membranes [16], [17]. It is our purpose in this paper to develop the non-equilibrium thermodynamics of small systems offering an interpretation of the non-equilibrium thermodynamics concepts as well as identifying the role played by dissipation.

3. Mesoscopic non-equilibrium thermodynamics [3], [4]

A reduction of the observational time and length scales of a system usually entails an increase in the number of nonequilibrated degrees of freedom. Those degrees of freedom, denoted by $\gamma \equiv (\gamma_i)$, may for example represent the velocity of a colloidal particle, the orientation of a magnetic moment, the size of a macromolecule or any coordinate or order parameter whose values define the state of the system in a phase space. The characterization at the mesoscopic level of the state of the system follows from $P(\gamma, t)$ the probability density of finding the system at the state γ at time t. To bring the system to a state characterized by certain value of γ , we need to exert work. The minimum reversible work required $\Delta W(\gamma)$ is given by

$$\Delta W = \Delta E - T\Delta S + p\Delta V - \mu\Delta M + y\Delta Y + ... \tag{4}$$

where E is the internal energy, S the entropy, V the volume, M the mass and μ the chemical potential. The last term stands for other types of work (electric, magnetic, surface work...) performed on the system, with y being the intensive parameter and Y its conjugated extensive variable [6]. The expression of the work reduces to the different thermodynamic potentials by imposing the constraints that define those potentials. For instance, in the case of a constant temperature, volume and number of particles, the minimum work corresponds to the Helmholtz free energy.

We will assume that the evolution of the degrees of freedom is described by a diffusion process in γ-space and formulate the corresponding Gibbs equation [19]

$$\delta S = -\frac{1}{T}\int \mu(\gamma)\delta P(\gamma,t)d\gamma \tag{5}$$

which resembles the corresponding law proposed in nonequilibrium thermodynamics for a diffusion process in terms of the mass density of particles. Here $\mu(\gamma)$ is a generalized chemical potential related to the probability density.

Alternatively, entropy variations can be computed from the Gibbs entropy postulate

$$S = S_{eq} - k_B \int P(\gamma,t)\ln\frac{P(\gamma,t)}{P_{eq}(\gamma)}d\gamma \tag{6}$$

where S_{eq} is the entropy of the system at the equilibrim state in which the probability density is given by

$$P_{eq} \equiv \exp(\frac{-\Delta W(\gamma)}{k_B T}) \tag{7}$$

where k_B is Boltzmann's constant. Taking now variations in (6) one obtains

$$\delta S = -k_B \int \delta P(\gamma,t)\ln\frac{P(\gamma,t)}{P_{eq}(\gamma)}d\gamma \tag{8}$$

where the variations of the equilibrium entropy are given by

$$\delta S_{eq} = -\frac{1}{T}\int \mu_{eq}(\gamma)\delta P(\gamma,t)d\gamma \tag{9}$$

and μ_{eq} is the value of the chemical potential at equilibrium. Comparison of both results leads to the identification of the generalized chemical potential

$$\mu(\gamma,t) = k_B T \ln\frac{P(\gamma,t)}{P_{eq}(\gamma)} + \mu_{eq} \tag{10}$$

which in light of Eq. (7) can also be written as

$$\mu(\gamma,t) = k_B T \ln P(\gamma,t) + \Delta W \tag{11}$$

The evolution in time of the system is then described by a generalized diffusion process over a potential landscape in the space of mesoscopic variables γ . The process is driven by the thermodynamic force

$$\frac{\partial}{\partial\gamma}\frac{\mu}{T} \tag{12}$$

The entropy production of the process is given by

$$\sigma = -\frac{1}{T}\int J\frac{\partial\mu}{\partial\gamma}d\gamma \tag{13}$$

or by using the expression of the chemical potential

$$\sigma = -k_B \int J(\gamma,t)\frac{\partial}{\partial\gamma}(\ln\frac{P(\gamma,t)}{P_{eq}(\gamma)})d\gamma \tag{14}$$

In this expression, we can then identify the thermodynamic forces as the gradient in the space of mesoscopic variables of the logarithm of the ratio of the probability density to its equilibrium value. The current and the force can be coupled linearly

$$J(\gamma,t) = -k_B L(\gamma, P(\gamma)) \frac{\partial}{\partial \gamma} (\ln \frac{P(\gamma,t)}{P_{eq}(\gamma)}), \tag{15}$$

where $L(\gamma, P(\gamma))$ is an Onsager coefficient, which in general depends on the state variable $P(\gamma)$ and on the mesoscopic coordinates γ. To derive this expression, locality in γ-space, for which only fluxes and forces with the same value of γ become coupled, has also been taken into account. The current can be substituted into the continuity equation

$$\frac{\partial P}{\partial t} = -\frac{\partial J}{\partial \gamma} \tag{16}$$

to obtain the kinetic equation

$$\frac{\partial P}{\partial t} = \frac{\partial}{\partial \gamma} (D P_{eq} \frac{\partial}{\partial \gamma} \frac{P}{P_{eq}}) \tag{17}$$

where the diffusion coefficient is defined as

$$D(\gamma) \equiv \frac{k_B L(\gamma, P)}{P} \tag{18}$$

This equation, which in view of Eq. (7) can also be written as

$$\frac{\partial P}{\partial t} = \frac{\partial}{\partial \gamma} (D \frac{\partial P}{\partial \gamma} + \frac{D}{k_B T} \frac{\partial \Delta W}{\partial \gamma} P) \tag{19}$$

is the Fokker-Planck equation for the evolution of the probability density in -space. Different forms of this equation follows from different expressions of the work done on the system. When the minimum work is given by the Gibbs free energy G , $\Delta W \equiv \Delta G = \Delta H - T\Delta S$, where H is the enthalpy, this equation transforms into the Fokker-Planck equation for a system in the presence of a free energy barrier:

$$\frac{\partial P}{\partial t} = \frac{\partial}{\partial \gamma} (D \frac{\partial P}{\partial \gamma} + \frac{D}{k_B T} \frac{\partial \Delta G}{\partial \gamma} P) \tag{20}$$

Other cases of interest concern different thermodynamic potentials. For instance, a particularly interesting situation is the case of a purely entropic barrier, often encountered in soft condensed matter and biophysics. In this case the kinetic equation is

$$\frac{\partial P}{\partial t} = \frac{\partial}{\partial \gamma} (D \frac{\partial P}{\partial \gamma} - \frac{D}{k_B} \frac{\partial \Delta S}{\partial \gamma} P) \tag{21}$$

We have seen that mesoscopic nonequilibrium thermodynamics provides a simple and direct method to determine the dynamics of a system from its equilibrium properties obtained through the equilibrium probability density.

4. Activated processes

Activated processes are those that need a finite energy to proceed and change the system from one state to another. The paradigm of activated processes is the crossing of a free energy barrier that separates two well-differentiated states that lie at the local minima at each side of the barrier. The system needs to acquire energy to surmount the barrier. Once the barrier is crossed, energy is released. Processes like thermal emission in semiconductors, chemical reactions, adsorption, nucleation, and active transport through biological membranes, share these features and, therefore, are generically referred to as activated processes. It is important to emphasize the essential difference between activated processes and the linear processes described by non-equilibrium thermodynamics. The latter constitute the response to the application of an external force or gradient and may emerge even at very low values of the applied force, in the linear response regime. Contrarily, the regime in which activated processes may take place is basically nonlinear. In this context, we can contrast the linear Fourier, Fick, or Ohm laws, in which the corresponding currents are proportional to the conjugated thermodynamic forces or gradients, with the exponential laws appearing in activated processes. Let us consider a general process for which a system passes from state 1 to state 2 via activation. Instances of this process can be a chemical reaction in which a substance transforms into another, an adsorption process in which the adsorbing particle goes from the physisorbed to the chemisorbed state, or a nucleation process in which the metastable liquid transforms into a crystal phase. Nonequilibrium thermodynamics describes the process only in terms of the initial and final positions and is valid only in the linear response regime. If we consider the process at shorter time scales, the state of the system progressively transforms by passing through successive molecular configurations. These different configurations can be characterized by a reaction coordinate γ. In this situation, one may assume that this reaction coordinate undergoes a diffusion process through a potential barrier separating the initial from the final states. It is often the case that at the time scales of interest the system is mostly found in the states 1 and 2, which correspond to the minima at and , respectively. The probability distribution is strongly peaked at these values and almost zero everywhere else. This happens when the energy barrier is much higher than the thermal energy and intra-well relaxation has already taken place. Using MNET, we will show that the Fokker-Planck description, under these conditions, leads to a kinetic equation in which the net reaction rate satisfies the mass action law.

The diffusion current in γ-space can be rewritten in terms of the local fugacity defined along the reaction coordinate

$$z(\gamma) = \exp \frac{\mu(\gamma)}{k_B T} \tag{22}$$

as

$$J = -k_B L \frac{1}{z} \frac{\partial z}{\partial \gamma} \tag{23}$$

where $D = k_B L/z$ represents the diffusion coefficient. We now assume that this coefficient is constant and integrate from 1 to 2, obtaining

$$\bar{J} = \int_1^2 J d\gamma = -D(z_2 - z_1) = -D(exp\frac{\mu_2}{k_B T} - exp\frac{\mu_2}{k_B T}) \tag{24}$$

This equation can alternatively be expressed as

$$\bar{J} = J_0(1 - exp\frac{A}{k_B T}) \tag{25}$$

where $\bar{J}$ is the integrated rate, $J_0 = D\exp(\mu_1/k_B T)$ and $A = \mu_1 - \mu_2$ is the corresponding affinity. We have then shown that MNET leads to nonlinear kinetic laws. This scheme has been successfully applied to different classical activated processes, like chemical reactions, adsorption, thermal emission in semiconductors, or nucleation, to obtain the corresponding kinetic laws.

5. Applications

The mesoscopic non-equilibrium thermodynamics theory presented here has been used to analyze non-equilibrium processes of different natures taking place in small-scale systems. In this section, we will mention some cases in which the theory has been successfully applied

Nucleation kinetics. The role played by translational and rotational degrees of freedom of the clusters in the nucleation kinetics has been analyzed by using the method of mesoscopic non-equilibrium thermodynamics [20]. It has been shown that the nucleation process is influenced by the dynamics of those degrees of freedom. The expression obtained for the nucleation rate differs from the value of this quantity obtained under the assumption that clusters are at rest. Consideration of mesoscopic variables relaxing in shorter time scales proposes a new scenario which provides a closer agreement with the experiments [21].

Transport through ionic channels. Entropic forces due the presence of constraints hampering the access of the system to certain regions play a very important role in many situations such as in the motion of biomolecules through pores, phoretic effects, transport through ionic channels and biological pumps and protein folding. The theory introduced here provides the expression for the diffusion current, the effective diffusion coefficient and the kinetic equation [22]. It has been shown that the diffusion coefficient obeys a scaling law and that the kinetic equation can be formulated under quasi-onedimensional conditions, considerably simplifying the analysis of the diffusion in complex structures.

Polymer crystallization. In many practical instances, polymer crystallization takes place under the influence of gradients. The metastable phase under this circumstance has its own nonequilibrium dynamics which is coupled to the crystallization processes. In the case of a velocity gradient [23], the resulting diffusion coefficient of the clusters depends on the shear rate, the pressure and the viscosity and shows anisotropy as found in experiments. These effects become particularly important for high shear rates and small or moderate pressures and when the system is close to the glass transition when the viscosity increases significantly.

Translocation of a biomolecule. Many biological processes involve the translocation of proteins or nucleic acids through pores or channels. It has been shown that diffusion drives the biomolecule very slowly in such a way that it would be unable to cross the pore. The presence of proteins binding to the biomolecule rectifies the diffusion and is responsible for the translocation process. The role played by those proteins in the process has been analyzed by considering the number of proteins as a new mesoscopic variable. The value of the resulting force agrees with simulations [24].

Active transport in biological membranes. Active transport across membranes is a crucial intermediate step in many biological processes for which ions move against their chemical potential fuelled by the energy released from the hydrolysis of the ATP. Mesoscopic non-equilibrium thermodynmics has been used to derive the nonlinear current for active transport of ions across a membrane [16] consistent with experimental observations. The theory has also been applied to explain the phenomenon of slippage in biological pumps [17].

6. Conclusions

In this paper we have shown how non-equilibrium thermodynamics can be constructed for the irreversible evolution of small systems. We have shown that mesoscopic nonequilibrium thermodynamics describes the irreversible behaviour of small-scale systems in which the presence of large fluctuations exerts an important influence on the dynamics. The theory uses the scheme proposed by nonequilibrium thermodynamics extending the concept of local equilibrium to the mesoscale [4] to show that not only the evolution of the mean values is described by nonequilibrium thermodynamics, as established by Onsager regression laws, but the evolution of the fluctuations as well. The applications to a broad variety of situations and the potential use in others show the usefulness of the theory in providing the mesoscopic dynamics of thermodynamic systems. Our analysis may provide a thermodynamic basis for experiments performed on small systems which operate under non-equilibrium conditions for which the absence of the thermodynamic limit and the importance of the fluctuations may constitute relevant factors in the characterization of their equilibrium and dynamical properties. Clusters, single molecules, small pumps and motors are cases where our theory could systematically be applied.

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